Footsteps of a New CRO Era in Turkey Driven by Enhancement and Increasing Clinical Trial Activities

The business of clinical trials is increasing in Turkey as a direct result of improving each element of the clinical trial planning and conduct process. This process involves efficient electronic submission and approval systems, competitive approval turnaround time, and governmental research and development incentives. Further to these improvements, high-technology support mechanisms for clinical supply management, warehousing and site management organisations have recently led to Turkey becoming one of the most rapidly developing and popular destinations for clinical trials. Without limitation, local and international pharmaceutical, biotechnology and medical device companies are able to conduct each phase and class of the trials; in particular Phase II – Phase IV clinical trials.

Historically, Phase III – IV studies constitute most of the clinical trials in Turkey. Recently, we started to see Phase I (first in man) studies being conducted in approved Phase I units.

A brief overview of the status of clinical trials in Turkey can be summarised as below:-

- Out of 1962 studies registered, 592 studies are ongoing (www.clinicaltrials.gov, September 2015)
- Compared to 978 trials registered in 2011 (www.clinicaltrials.gov, February 2015), there has been a significant rate of increase in the clinical trial industry over recent years.

This rate of increase places Turkey, along with China and South Korea, in the top three countries to have the fastest rate of increase in clinical trial registrations.

According to the Tenth Development Plan published by the Turkish Ministry of Development, the 2014-2018 Healthcare Related Industries Structural Transformation Program Component-2: Developing R&D and Innovation Fields describes plans to:-

- Increase the number of Turkish and foreign qualified researchers
- Establish accredited research test measurement centres which will work in close cooperation with both domestic and foreign private sectors
- Design programmes for sustainable R&D

Responsible parties (Ministry of Science, Industry and Technology, Ministry of Development, Ministry of Health) have set the goals in line with governmental targets for clinical trials. The table at the bottom of the page shows the projected figures.

Setting a strategic goal to increase the number of clinical trials at governmental level is critically important.

The organisations working in the clinical trial industry will be expected to operate in line with these strategic objectives.

Furthermore, the following practices have been put into effect in order to provide the perfect environment for achieving these goals.

- Acceptance of a single ethical review for multi-centre human health and medical research
- Adoption of in-common policies, procedures and forms
- A relatively quick import licence approval process
- Introduction of guidelines on clinical trials; including a 15-day timeframe for ethics, a 30-day maximum timeframe for governance review and, most importantly, the possibility of a parallel submission process

Beyond these important improvements, the quality of both academic clinical leaders and healthcare infrastructure, and the large and ethnically diverse, informed population, make Turkey a good location for all stages of clinical trials. Global rationalisation trends of industry and emerging competition from lower-cost centres are likely to be an advantage to Turkey's long-term competitiveness as a destination for clinical trials run by the global pharmaceutical, biotechnology and medical device industry.

The increase in the number of clinical trials due to the factors outlined above, have in turn generated the ongoing growth of the CRO market in Turkey.

Recently, the number of both local and international CROs has increased significantly. As Turkey develops innovative and fast implementation approaches, relevant organisations are enabled to achieve the strategic goals set forth at government level. CRO business will continue to rise in parallel with the number of clinical trials.

The reasons behind the issuing of further regulations on contract research organisations (as drafted on July 2015 by the Ministry of Health and Medical Drugs and Medical Devices Agency) include:-

- Concerns regarding the fact that the significant increase in the number of CROs may have an effect on the quality

No	Indicator	2013	2014	2015	2016	2017	2018
1	Clinical Trial Investment (million $/ year)	85	96	120	149	189	234
2	Clinical Trial Numbers	407	460	570	715	900	1125

of working practices
- Inadequate clinical trial professional employment potentially posing a threat to human health and quality of data

This draft regulation outlines the clear requirements on all contract research organisations and research professionals.

The key points of the new CRO draft regulation are briefly stated below:

"Responsible company executive must have at least five-years (5) experience in the clinical trials field… CRO companies which provide a monitoring service should employ 2 CRAs with at least 2 years' experience who must have been certified as clinical research professionals…; a separate quality department must have been established with at least 1 quality officer… study spaces, a meeting room, controlled archive units where records may be tracked must be present… standard operation procedures in accordance with the relevant regulation must be present…

One of the key changes in the new draft regulation will be the clause stating "self employed companies cannot refer to themselves as Contract Research Organizations".

All new and current CROs must apply to the government with the relevant documents demonstrating that all requirements are met. Furthermore, all CROs must obtain competency certification from the Turkish Drug and Medical Devices Institution, and declare they will prove their competency every 12 months. In case there is a failure to comply with all of the requirements, the aforementioned Institution has the right to suspend or void the license of the CRO.

If the regulation is approved, CROs failing to comply with the requirements will be terminated, and it will not be possible to provide or obtain a CRO service by freelancing as a private company. The multinational CROs planning to penetrate into the CRO market in Turkey must be prepared for the new governmental legislation, and in particular they must ensure that their SOPs are in accordance with the local regulations.

If the draft regulation which is set forth – including legislation to standardise quality and service and several training and competency requirements – is approved, it is currently unknown whether, in its current form, it is completely feasible, or indeed possible, to enforce the new requirements.

Potential obstacles regarding the new legislation aside, it is important to note that Turkey was the first country that accredited CROs by inspecting them in terms of GCP and quality systems, and, in this way alone, has served as a model for other countries.

Taking into account the huge responsibility of CROs regarding human health and safety and the protection of rights of subject and sponsor, it is appropriate that not only Turkey, but all countries, set out the minimum qualities required for organisations carrying out such important work, and inspect these organisations against the requirements on an ongoing basis.

The vast scope and clarity of the new regulations outlined by the Turkish Drug and Medical Devices Agency, including inspection, training and approval processes, should be a prerequisite of all countries with an existing or growing clinical trials industry. Clinical trial projects are typically long-term and thus, the regulation established must be systematic, time-sensitive and sufficiently explicit. It is essential that the new legislation allows for operating methods which are sustainable within the precise and time-sensitive industry of clinical trials. If the new regulations cannot meet this requirement, the new legislation will be unable to achieve its goal regarding improving the quality standards of increasing clinical trial activities in Turkey.

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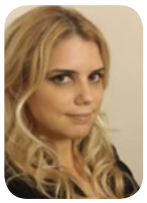

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